Sleep Science and Fatigue Risk Management:

Testimony to the Committee on Transportation and Infrastrucure's Aviation Sub-Committee

regarding the Pilot Flight and Duty Time Rule

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Abstract

Fatigue risk management applies 1) the science of sleep, frequently as instantiated into mathematical modeling, 2) the tactics, techniques, and procedures of sleep and performance measurement in the operational environment, complemented by 3) the clinical practice of sleep medicine to reduce the risks of poor performance, lost productivity, and error, incident and accident in the workplace. As envisioned here, fatigue risk management in aviation will in the short-term improve performance, productivity and safety and in the longer term improve flight crew and other commercial aviation operational personnel health and well being.

Introduction to Fatigue Risk Management

Fatigue risk accrues from the extended work hours, early starts, and the shift work necessary to staff 24x7 operations. This is visibly apparent in Figure 1, a composite image of the earth at night.

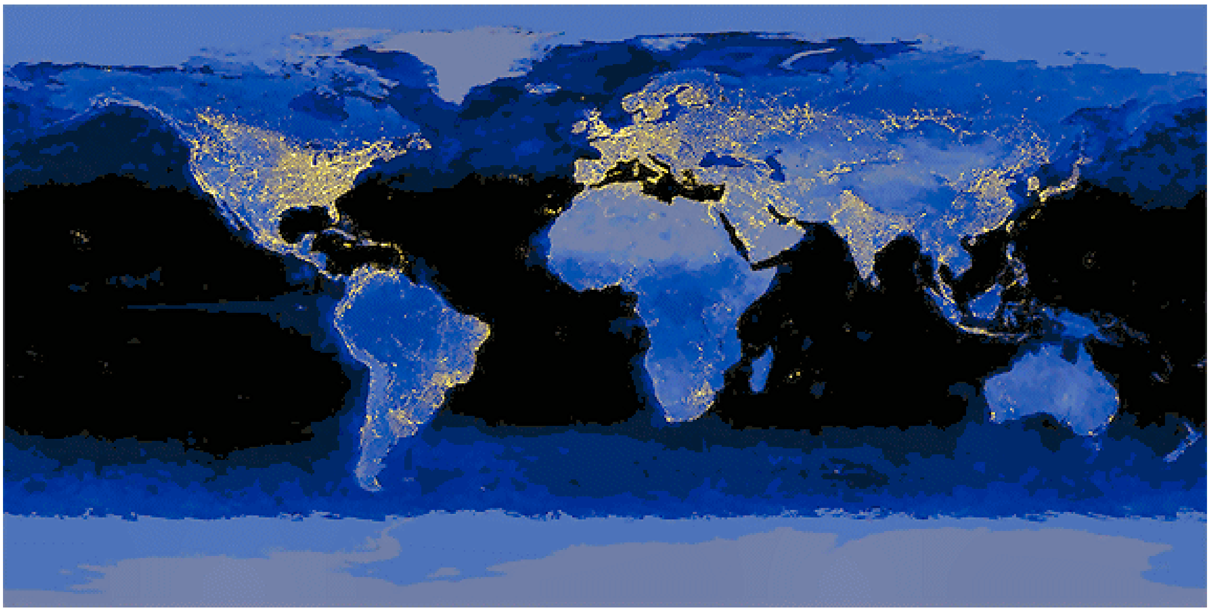

Figure 1:   A composite image of the earth at night graphically illustrating the extent of 24x7 operations and the reality driving the need for extended work hours, early starts, and shift work. *Courtesy of NASA*

Fatigue risk management applies sleep science and the clinical practice of sleep medicine to reduce fatigue and improve performance, productivity, safety, health, and well-being in the workplace (Belenky and Akerstedt, in press). By mitigating the "fog of fatigue", it enables the management of fatigue risk (Moore-Ede, 1995). Error, incident, and accident causation in any particular case is multi-factorial, complex, and tightly-coupled (involving multiple, interdependent, linked processes) (Perrow, 1999). With respect to any particular accident, ascribing a causal role to fatigue is difficult (Hersman, 2010), nevertheless an increase in fatigue appears to shift the performance distribution toward increased risk, making error, incident, and accident more probable and decreasing the likelihood of recovery even if the error is detected (Thomas, et al., 2007;Van Dongen, et al., 2010).

Applying the science of sleep enables fatigue-friendly rostering and scheduling and other fatigue-related “anti-fogmatics”, otherwise known as fatigue countermeasures, that blunt the adverse effect of extended work hours, shift work, and cumulative fatigue on performance, productivity, health, and well being. Applying the clinical practice of sleep medicine in the occupational setting enables the assessment of sleep disorders and their effects on alertness, performance, productivity, and safety in the workplace and their detection, treatment, and evaluation of treatment outcome.

Fatigue risk management has both short and long-term horizons. The short-term horizon is framed in terms of reducing the immediate risk of error, incident, and accident (Gander et al., in press). The long-term horizon is framed in terms of improving health and well being across a person’s working life, particularly in reducing obesity, insulin resistance, metabolic syndrome, type II diabetes, hypertension, cardiovascular disease, and cognitive decline (Van Cauter, et al., 2008; Mullington, et al., 2009).

One way of applying the science of sleep to create fatigue-friendly rosters and schedules involves integrating sleep and fatigue-related experimental findings, technologies, and metrics as components of personal biomedical status monitoring. In the not too distant future, personal biomedical status monitoring will be available to measure and integrate a plethora of parameters, including metabolic indices (e.g., blood glucose, caloric expenditure); cardiovascular parameters (e.g., blood pressure, EKG, and arterial intima function); inflammatory markers (e.g., leukocytes, IL-6, and high sensitivity C-reactive protein); behavioral metrics (e.g., sleep/wake history, circadian rhythm phase and amplitude); metrics of cognitive performance (e.g. reaction times, memory); and workload (e.g., time on task and metrics of task intensity). Personal biomedical status monitoring will form the basis of open- and closed-loop systems to monitor and intervene when necessary, in order to sustain human health, well-being, and operational performance. With respect to operational performance, biomedical status monitoring will provide diagnostics and prognostics for the person in the operational loop by supplying inputs (e.g., sleep/wake history, circadian phase, and workload) to mathematical models to predict individual performance in real-time. These predictions will be benchmarked against, and individually adjusted to predict, actual performance (Olofsen, et al., 2004), and used as the evidence-base for real-time fatigue risk management.

To make a military analogy, sleep can be viewed as an item of logistic resupply with respect to sustaining operational performance. In managing fuel consumption, a battalion logistics officer can measure how much fuel the battalion has on hand, apply a simple mathematical model taking as input miles to be driven and estimated mileage by vehicle type to estimate how long this fuel will last, and with this estimate in hand plan for timely resupply. Similarly in managing sleep-loss related fatigue, one can measure sleep/wake history in operational personnel using actigraphy, and use this sleep/wake history as input to a mathematical model predicting how long this sleep will sustain individual performance. In light of these predictions, one can adjust operations to ensure timely resupply of sleep, by arranging a sleep opportunities of adequate length and sleep-conducive circadian placement. Eventually, models will integrate individual performance predictions to predict work group performance.

Components of fatigue and relation to fatigue risk management

Fatigue is a function of the interaction of multiple factors including sleep/wake history, circadian rhythm phase, and workload, and is modulated by individual differences in response to these factors (Wesensten et al., 2004; Van Dongen, et al., 2005). A fatigue-inducing factor is one that shifts the fatigue-risk distribution in the direction of increasing risk of error, incident, or accident. Figure 2 shows experimental data capturing the interaction of sleep/wake history (in this instance, of total sleep deprivation), circadian rhythm phase, and time on task (a component of work load) on cognitive performance (Wesensten et al., 2004). Individuals vary one from another in their sensitivity to these factors (Van Dongen, et al., 2005). This relative variability in sensitivity to sleep loss appears to be an enduring individual trait (Van Dongen, et al., 2005). Thus, the ability of an individual to perform in the workplace varies over time as a function of, at a minimum, sleep/wake history, circadian rhythm phase, workload, and the trait-like individual variability in sensitivity to these factors. Measuring/estimating these parameters and integrating their effects on performance through mathematical modeling can provide the basis for effective fatigue risk management systems (FRMS).

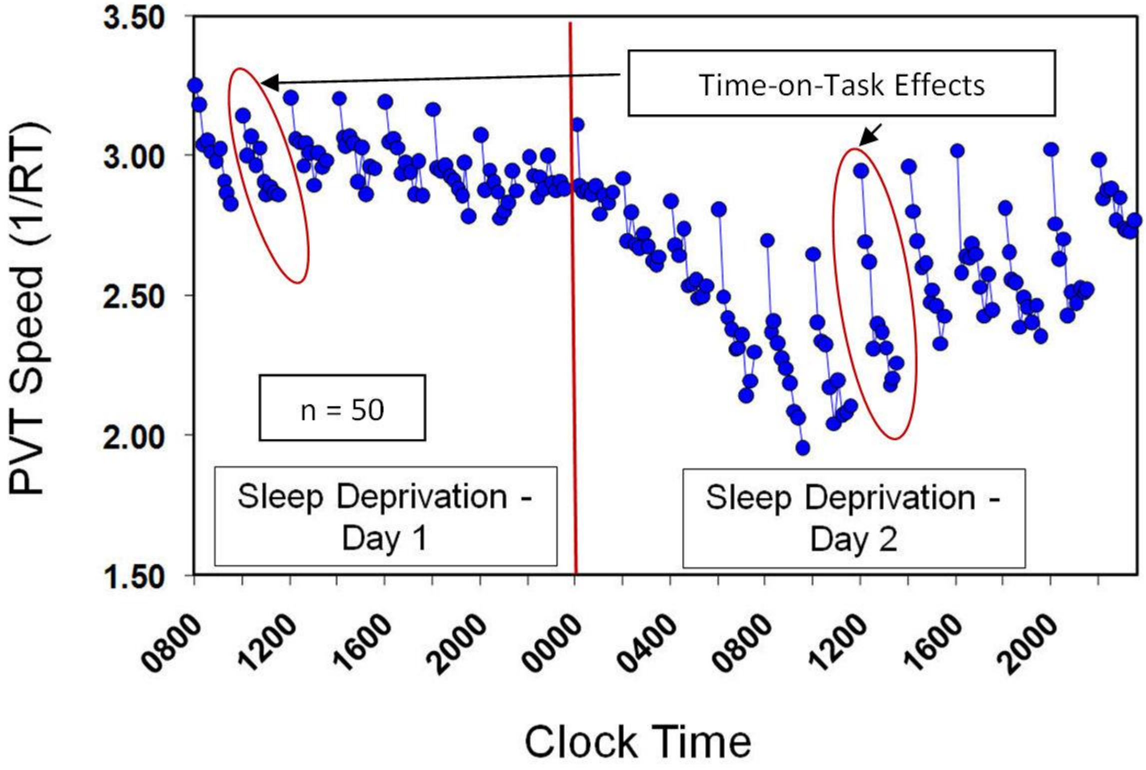

Figure 2: The effect of fatigue (a combination of time awake, time of day, and time on task) on psychomotor vigilance task (PVT) performance (expressed as the inverse of reaction time (1/RT)) in 50 healthy particpants (13 women) (age range 18-30 years; mean = 22.4) deprived of sleep for 40 consecutive hours. Time awake and time on task degraded performance and this degradation was modulated by the circadian rhythm (time of day). Note the amplification of the time on task effect (red ellipses) by time awake and time of day. *Adapted from Wesensten, et al., 2004.*

Measuring fatigue

Fatigue is operationally defined subjectively by self-report and objectively by degraded alertness and task performance (McDonald et al., in press). Self-report of fatigue consist of a verbal response (e.g., the subject says "I am tired") or a written response (e.g., by marking the Samn-Pirelli Fatigue Scale) (Samn and Perelli, 1982). Degraded operational task performance can be measured by a variety of tasks, some more sensitive than others (Balkin et al., 2004). The psychomotor vigilance task (PVT) is particularly sensitive to attentional lapses and has other desirable psychometric properties (Dinges and Powell, 1985; Balkin et al., 2004; Dorrian et al., 2005). There are neurophysiological correlates of fatigue as well, such as polysomnographically measured sleep latency (Carskadon, et al., 1986). Tasks such as the PVT are not intrinsic to workplace performance but are <u>added metrics</u> that to acquire takes a person away from the actual work the person is doing (McDonald, et al., in press). In contrast, <u>embedded metrics</u> are metrics that are taken from actual workplace performance, are seamless and invisible, and therefore do not interrupt the normal flow of work (McDonald, et al., in press). An example of such an embedded metric is lane deviation as an indicator of driver performance in the commercial trucking industry. Lane deviation can be measured effectively in both simulation and in real world, over-the-road operations (Philip, et al., 2005). Another embedded metric, fuel economy, may also be modulated by fatigue (Van Dongen, et al., 2010). Other systems, such as flight operational quality assurance (FOQA) in commercial aviation, may provide useful information about performance. We humans increasingly find ourselves embedded in robotic and automated systems, especially in the workplace – "… all watched over by machines of loving grace" in the words of the poet, Richard Brautigan (http://www.redhousebooks.com/galleries/freePoems/allWatchedOver.htm) – and as a result embedded performance metrics will be increasingly available across a variety of workplaces and operational platforms.

Sleep, Circadian Rhythm, Workload, the Operational Environment, and Operational Performance

Sleep, sleep loss, and measuring sleep/wake history

Total sleep deprivation and chronic partial sleep restriction (collectively, sleep loss) leads to fatigue. Fatigue from sleep loss yields degraded efficiency and productivity at work and leads to increased errors, incident, accidents, and economic loss. These economic losses accrue to employers, employees, and to society (Folkard, et al., 2005). In the longer term, there is increasing evidence that sleep loss is associated with adverse effects on mental and physical health, such as weight gain and obesity (Knutson, et al., 2007), hypertension and cardiovascular problems (Meir-Ewert, et al., 2004) gastrointestinal disease, chronic fatigue, substance/alcohol abuse, family problems, and mood difficulties (Costa, et al., 2004). Thus, the adverse effects of sleep loss include both immediate and longer term effects.

In laboratory studies both acute, total sleep deprivation and chronic, partial sleep restriction lead to decrements in task performance, well-being, and health. Acute, total sleep deprivation degrades cognitive performance linearly over days, modulated within days by the circadian rhythm, with an average over the each day loss of capacity useful task performance of 17-25% per day (Thorne, et al., 1983; Thomas, et al., 2000). Mild, moderate, and severe sleep restriction (7, 5, or 3 hours time in bed/night for 7 days, respectively) leads to sleep-dose-dependent decreases in performance over time in comparison to baseline or to sleep augmentation (9 hours time in bed/night) (Belenky, et al., 2003) (see Figure 3). For 7 and 5 hours time in bed/night, performance appears to stabilize at lower levels after 3-4 days while for the 3 hours time in bed/night performance continues to degrade across the 7 day experimental period. In a complementary study of chronic sleep restriction, 6 and 4 hours time in bed/night for 14 days led to sleep-dose-dependent degraded task performance (Van Dongen, et al., 2003). Of clear operational importance is the finding that even mild sleep restriction (7 hours time in bed/night) degrades performance over time (Belenky, et al., 2003). In the first mentioned study (Belenky, et al., 2003), at the end of the 7 day sleep restriction period participants were allowed 8 hours time in bed/night recovery sleep for 3 nights. In contrast to acute total sleep deprivation, where recovery is complete in 1-2 days, performance in the 7, 5, and 3 hour time in bed groups did not recover to baseline task performance over the 3 day recovery period. This is of operational importance as chronic sleep restriction is common, not to say ubiquitous, and total sleep deprivation is rare. In a follow on study to the sleep restriction and recovery study described above, it was found that that preloading/augmenting sleep prior to the sleep restriction yielded more rapid recovery (Rupp, et al., 2008).

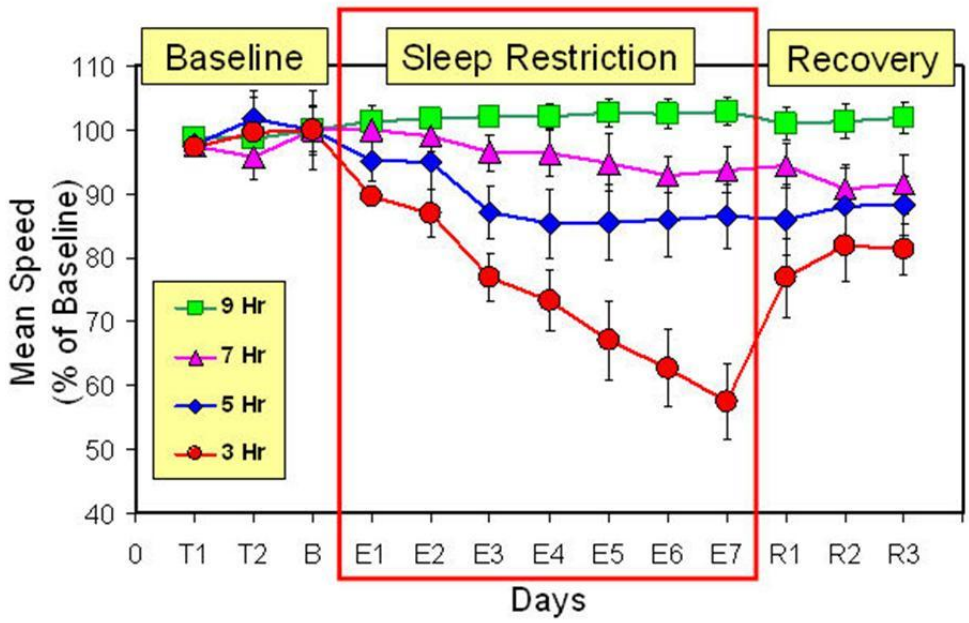

Figure 3: The effect of three levels (conditions) of sleep restriction (3, 5, or 7 hours time in bed/night) and one level (condition) of sleep augmentation (9 hours time in bed/night) over seven days (E1-E7) and compared to baseline (8 hours time in bed/night; B) and recovery (again 8 hours time in bed/night; R1-R3) on psychomotor vigilance task (PVT) performance (expressed as the inverse of reaction time (1/RT)) in 68 healthy adults (16 women) (age range 24-62 years; mean age = 37.3; 16-18 participants per sleep condition). *Adapted from Belenky, et al., 2003.*

The laboratory standard for measuring sleep/wake history is polysomnography (PSG), which uses the combination of electroencephalogram (EEG), electrooculogram (EOG), and electromyogram (EMG) to score total sleep time, sleep efficiency (% of sleep opportunity spent asleep), and the stages of sleep (N1, N2, N3, and REM). While PSG has been applied to recording and scoring sleep/wake history in the field, its dependence on an electrode array makes it impractical in most field settings. In field studies of sleep and performance, sleep diaries have been used but do not reliably measure total sleep time or sleep efficiency. In contrast to PSG and sleep diaries, the actigraph (a wrist-worn device containing an accelerometer, signal processing hardware and software, and memory) is comparable to PSG in measuring total sleep time and sleep efficiency (Ancoli-Israel, et al., 2003). The actigraph is a device about the size of a sports watch. Using its accelerometer, the actigraph measures arm movements and sums and records them typically in one-minute bins. From this activity record, using a validated against PSG sleep-scoring algorithm, a sleep/wake history for 30 consecutive days can usually be obtained before the device needs to be downloaded. Battery life and memory capacity are the limiting factors in the length and temporal resolution of the actigraph in collecting sleep/wake history. The actigraph is a useful tool for conducting field measurements over extended periods (days, weeks, months) and may have utility when combined with mathematical modeling when applied to fatigue risk management.

The circadian rhythm and measuring circadian rhythm phase

The circadian rhythm, a sinusoidal, 24-hour rhythm in core body temperature, sleep, and task performance, is set by the suprachiasmatic nucleus (SCN) of the hypothalamus, the endogenous biological clock in the brain (Moore, et al., 2002) (see Figure 4). The SCN itself receives direct input from the retina of the eye and responds to blue light with a distinctive phase response curve (Wright, et al., 2005). Core body temperature peaks around 2000 hrs and reaches its nadir between 0400-0600 hours. The circadian rhythms in task performance and sleep propensity parallel the circadian rhythm in core body temperature. Task performance peaks in mid-evening just subsequent to the peak in the circadian temperature rhythm and troughs in the early morning just subsequent to the trough in circadian temperature rhythm. Sleep propensity follows the circadian rhythm in core body temperature making it difficult to fall asleep and to stay asleep when core body temperature is rising or high and easy to fall asleep and to stay asleep when core body temperature is falling or low. The circadian rhythm modulates the risk of injury, a correlate of degraded performance. Risk of injury increases depending on the shift worked, with the lowest rates of injury risk on morning shifts and highest rates on night shifts (Folkard and Tucker, 2003). Thus, injury rates on the job are highest during the late night/early morning circadian low (Folkard and Tucker, 2003). Mild to moderate sleep loss, common for night shift workers who typically experience restricted sleep during the day (Akerstedt, 2003), leads to decrements in performance (Belenky, et al., 2003). Sleep/wake history and the circadian rhythm interact to affect alertness, sleep propensity, and performance.

Figure 4: The circadian rhythm in core body temperature. Performance follows the temperature curve, peaking just after the peak in temperature. Sleep propensity follows the inverse of the temperature curve, peaking when body temperature is lowest. *From Kryger, Roth and Dement, 2005.*

The laboratory standard for measuring circadian rhythm phase is dim light melatonin onset (DLMO) (Lewy and Sack, 1989). Measuring DLMO requires laboratory control and dim light and is not suitable for field measurement. An alternative metric to DLMO is core body temperature measured by swallowable temperature pill or rectal probe (Edwards, et al., 2002). Because of masking effects of movement, core body temperature measurements require laboratory control and constant routine and are also not suitable for field measurement. In a person habituated to a particular time zone, circadian phase can be estimated in the field by self report on the basis of the local time zone alone. However, in crossing time zones any predictability by self report is destroyed because of the sensitivity of the SCN to light exposure in the early morning and late afternoon/early evening hours. The cross over point of the phase response curve of the SCN in a person habituated to a local time zone is in the temporal vicinity of 0300 hours, the midpoint of subjective night (Moore, 1997). In an individual habituated/synchronized to a time zone, exposure to light before the crossover point of the phase response curve is seen by the SCN as a late sunset and stimulating a circadian phase delay, while exposure to light after the crossover point is seen by the SCN as an early dawn stimulating a circadian phase advance. The maximum phase response (shift in circadian phase) to light exposure is at dawn and dusk. This variability in the phase response curve makes the prediction of shifting phase angle by self-report when crossing multiple time zones difficult without exact knowledge of initial circadian phase and light exposure at the level and position of the eye. In theory, and perhaps in practice, accurate measurement of light exposure at the level and position of the eye combined with accurate mathematical models describing the SCN phase response curve to light may enable the accurate prediction of circadian phase with shifting time zones (Bierman, et al., 2005).

Workload

Workload is not satisfactorily operationally defined and therefore not easily measured in either laboratory or field. Some studies have equated workload with time on task, a component of workload. Fatigue as a result of time on task has been shown to be relieved by breaks within shift (Knutson, et al., 2007). Thus, fatigue from time on task recovers with simple rest, a break from task performance, and does not require sleep to recover. In contrast, fatigue and performance decrements related to time awake are only reversed by sleep (Dawson and McCulloch, 2005). Fatigue resulting from working long hours or overtime shifts increases the risk of accident (Dembe, et al., 2005). Workload, time of day, and sleep loss all interact to affect task performance.

The operational environment

The operational environment is defined as a work setting in which human task performance is critical and if human performance degrades the system will fail. In the operational environment, the human-in-the-operational-loop has limited time to decide and act (Wesensten, et al., 2005). There are a large variety of operational settings. These include military operations, maritime operations, medicine, the modes of land transportation, aviation, security work, energy generation, resource extraction (mining and drilling), financial markets, and industrial production. In brief, any 24x7 operation and any operation involving extended work hours or shift work is an operational setting. In these settings, the operational characteristics described previously (i.e., shift timing and duration, work intensity, and difficulty and complexity of the work tasks) degrade performance directly through the effects of workload and/or working through the circadian low and indirectly by reducing the amount of time available for sleep or placing the sleep opportunity at a non-propitious time for sleep, thus reducing total sleep time, a primary determinant of alertness and performance (Wesensten, et al., 2005). The effects of fatigue on real-world or realistically-simulated operational performance can be complex. In an aviation simulation study, after completing a multi-day international run (fatigued) versus coming into the simulation after a few days at home (rested), Boeing 747 2-pilot crews were better able to detect errors but less able to manage them successfully (Petrilli, et al., 2007).

Operational task performance

This finding of degradation in complex task performance seen in simulator studies is complemented by evidence from laboratory studies in which some forms of complex task performance are degraded more than simple task performance (Harrison and Horne, 2000; Nilsson et al., 2005). There is however counter-evidence suggesting further subtleties (Tucker et al., 2010). Evidence from imaging studies suggests total sleep deprivation selectively deactivates the prefrontal cortex as indicated by a larger decrease in glucose uptake (regional cerebral metabolic rate glucose (rCMRglu) than the rest of the brain as measured by positron emission tomography using 18-fluoro-2-deoxyglucose as tracer (Thomas et al., 2000). This decrease in rCMRglu reflects a general decrease in neuronal firing as the brain depends on just in time delivery of glucose and, then, oxygen (Magistretti, et al., 1995). As the prefrontal cortex is responsible for complex task performance, including judgment, planning, situational awareness and the integration of reason with emotion, this physiological evidence supports the behavioral findings under conditions of sleep loss (Harrison and Horne, 2000).

In complementary fashion, evidence from other imaging studies suggests that the prefrontal cortex is selectively targeted for recuperation during sleep, as the prefrontal cortex remains deactivated during both non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep, while the rest of the brain returns to approximately waking levels of activation during REM sleep.

A case example in which complex task performance degraded more than simple task performance comes from the debriefings conducted by one of the authors (GB) of friendly fire incidents during the 1990-1991 Gulf War (Operation Desert Storm). In one such incident, sleep restriction contributed to Bradley Fighting Vehicle crews losing their orientation to the battlefield (a complex task) and therefore causing them to mistake friend for foe while maintaining their ability to lay cross hairs on the target and shoot accurately (a simple task) resulting in the destruction of a friendly Bradley (Belenky et al., 1996).

Consolidated sleep, split sleep, and sleep fragmentation

Split sleep, in the form of biphasic sleep, occurs naturally in cultures in which people regularly take siestas (Webb and Dinges, 1989). Recent studies have demonstrated that performance is a function of total sleep time in 24 hours, regardless of whether the sleep is consolidated or split (Belenky, et al., 2008) and irrespective of sleep stages (e.g., NREM and its stages or REM sleep). Thus, it does not appear to matter whether sleep is obtained in a single, consolidated sleep bout or distributed in 2 or 3 bouts over 24 hours (split sleep). Given equal total sleep time, split sleep appears to sustain performance as well as sleep consolidated into a single sleep bout (Belenky, et al., 2008). Thus, total sleep time measured by actigraphy can be used to predict performance in operational settings (Ancoli-Israel, et al., 2003).

Similarly, in some work settings involving night shift work and/or early starts, splitting sleep into main sleep period and supplementary naps is common. In a field study of physicians in training, assessing sleep and performance and comparing when working night float versus day shift, physicians averaged about 7 hours of total sleep time by actigraphy per 24 hours in both night float and day shifts (McDonald, et al., 2009). However, they obtained this sleep quite differently depending on which type of shift they were working. If working the day shift, the physicians obtained their 7 hours of sleep at night in a consolidated main sleep. If working night float, the physicians split their sleep and obtained their 7 hours of sleep in a main morning sleep of approximately 4 hours, supplemented with night time naps totaling 3 hours. Performance on the PVT, taken at approximately the same clock times going on and going off shift, was the same on night float and day shift.

Split sleep (2-3 multi-hour sleep bouts across a 24 hour period) should be clearly distinguished from fragmented sleep (sleep interrupted every few minutes). Sleep fragmented with even subliminal arousals (change in sleep stage in response to a stimulus) at a frequency of every 2-3 minutes can lose all recuperative value (Bonnet and Arand, 2003). In contrast, it appears that sleep bouts greater than 20 minutes in length have minute by minute recuperative value equivalent to consolidated sleep (Bonnet and Arand, 2003).

[L1] Individual differences in response to factors causing fatigue

There are substantial differences between individuals in degree of performance degradation resulting from sleep loss (Van Dongen, et al., 2005). These differences appear to be enduring characteristic that is present on subsequent retest, and therefore trait-like. Recent work has associated this trait-like difference with genetic markers (Viola, et al., 2007). There are also cohort differences associated with age. Older individuals perform less well than younger individuals when both are rested but perform better than younger individuals when sleep-restricted (Bliese, et al., 2006). There are individual differences in phase angle and amplitude of circadian rhythm which are likely to affect fatigue as measured by self-report and objective performance measures.

Predicting performance from the components of fatigue

In the 1980s, one of the authors (GB) was directing the U.S. Army's research program in sleep and performance, measuring sleep in the field environment by actigraphy. Actigraphy was a young, developing technology. When presented with early field actigraph studies, U.S. Army General Maxwell Thurman (General "Max") harrumphed and said, "I don't care how much they sleep, I want to know how well they perform." An actigraphically recorded sleep/wake history is a marvel of applied information technology, but in and of itself an actigraphically-derived sleep/wake history does not speak directly to the actigraph wearer's performance. Keeping General Max's response in mind, we developed a mathematical model taking sleep/wake history and estimated circadian phase as its inputs and yielding a minute-by-minute prediction of performance as its output. Our model and other similar models have become commercial products with application in the developing field of fatigue risk management (Wesensten, et al., 2005; Mallis, et al., 2004). General Max would be pleased – with actigraphy we will know how much people sleep and applying mathematical models to the actigraphic data we will be able to predict how well they will perform.

Systems of fatigue risk management

Outline of a fatigue risk management system (FRMS)

The traditional technique for managing fatigue risk in the workplace has been and still to a large extent is hours of service regulations. Hours of service rules were first promulgated in early 19th century Britain in response to the industrial revolution (Cornish and Clark, 1989). Such regulations typically specify the number of permissible hours on duty in 24 hours and sometimes weekly or other longer term limits as well. They take into account homeostatic sleep drive but not the effects of the circadian rhythm on performance and sleep propensity. Such rules are prescriptive and hence rigid and, as a defense against fatigue risk, are brittle. As there is a negative correlation between work hours and hours of sleep, i.e., longer work hours predict less sleep (Basner, et al., 2007; McDonald et al., 2008), this approach, as a broad first cut, has merit for normal day shift work where the person works during the day and sleeps at night. It is worth noting that employees who work afternoon shifts sleep more than employees working standard day shifts (Lauderdale, et al., 2006). When work and sleep are in harmony with the circadian rhythm in sleep propensity and performance, hours of service regulations are a reasonable approach. Where prescriptive rules breakdown are when the work schedule involves extended work hours, early morning starts, or night shifts as these simple prescriptive rules do not take into account the circadian rhythms in performance and sleep propensity.

The National Transportation Safety Board (NTSB) has taken an active role in working to reduce errors, incidents, and accidents in aviation by recommending a move away from simple prescriptive rules toward a system for managing fatigue risk that takes into account not just the effects of time awake but seeks to "set working hour limits for flight crews, aviation mechanics, and air traffic controllers based on fatigue research, circadian rhythms, and sleep and rest requirements" (http://www.ntsb.gov/recs/mostwanted/aviation_reduce_acc_inc_humanfatig.htm). More recently, The Honorable Deborah Hersman, the Chairman of the NTSB, has expressed support for moving beyond working hour limits to full-on fatigue risk management (http://www.ntsb.gov/speeches/hersman/daph100305.html).

In contrast to prescriptive hours of service regulation, evolving fatigue risk management systems are a flexible, multi-layer defense in depth against fatigue risk. In one conceptualization (Dawson and McCulloch, 2005), an organizational FRMS would include tactics, techniques, and procedures to ensure that employees have an adequate sleep opportunity both in terms of total sleep opportunity duration over 24 hours and in terms of placement relative to the circadian rhythm in sleep propensity. Further, it would measure (e.g., by sleep diary or wrist-worn actigraph) the use made by employees of the sleep opportunity that was available to them. Finally, given the sleep opportunity and the use made of it, an FRMS would evaluate (e.g., by self- or co-worker report, or with added or embedded performance metrics, or model-based performance predictions) how well employees are performing in the workplace while on duty.

Creating and implementing fatigue-friendly rosters and schedules

An FRMS can be implemented in a variety of forms from the technologically simple to the technologically complex. FRMS in Air New Zealand has been in use for around 15 years, overseen by a collaborative group with a combination management, crew member, and scientific/medical membership. The process originally consisted of soliciting and reviewing voluntary fatigue reports from pilots and flight attendants, and undertaking specific studies on highly reported trips or duties; these studies used a combination of subjective ratings such as the Samn-Perelli fatigue scale (Samn and Perelli, 1982), along with reaction time based performance tests. More recently, studies have asked pilots to complete a Samn-Perelli assessment just prior to descent (at top of descent), on a routine basis, and on some fleets this is being inputted directly into aircraft flight management computers. In FRMS such as the one used by Air New Zealand, the fatigue data collected is typically used to refine specific flights and schedules within the framework of existing prescriptive hours of service regulations (Petrie, et al., 2004; Powell, et al., 2008). easyJet has evolved a more complex system involving a detailed fatigue report form, as well as actigraphically-measured sleep/wake history, and FOQA data that is used to obtain specific exceptions to prescriptive hours of service regulations (http://www.faa.gov/about/office_org/headquarters_offices/avs/offices/afs/afs200/media/aviation_fatigue_symposium/StewartComplete.pdf). Most recently, Boeing has entered the FRMS field by integrating mathematical modeling predicting fatigue risk from sleep/wake history and circadian rhythm phase into commercial rostering and scheduling software produce what potentially could be a turnkey fatigue risk management system (Romig and Klemets, 2009). In FRMS such as being developed by Boeing, the model has the potential to become the rule, replacing prescriptive hours of service regulations.

Whether operating within prescriptive rules, used to obtain relief from specific aspects of prescriptive rules, or replacing prescriptive rules, implementation of an FRMS occurs within a complex context, e.g., regulatory environment, labor/management agreements, economic imperatives, and organizational structure. There are synergies if FRMS is implemented in the context of broader safety and operational risk management. The aim of FRMS is to maximize on shift performance and total sleep time in 24 hours within existing operational constraints.

Screening, diagnosing, and treating sleep disorders

A common cause of degraded performance and excessive day time sleepiness is inadequate sleep. Inadequate sleep can result from a number of factors including sleep disorders - in particular, obstructive sleep apnea (OSA). OSA is a respiratory impairment characterized by severely disturbed breathing during sleep due to the blockage of airflow in the upper airway (Carskadon and Dement, 1981). This results in frequent arousals triggered by the drive to breathe, causing fragmentation of sleep which degrades its recuperative value, and leads to performance impairments and excessive day time sleepiness (Adams et al., 2001; Lavie, 1983). For instance, patients suffering OSA experience often report falling asleep briefly when stopped at traffic lights or while sitting quietly on the couch in the afternoon (Johns, 1993; Johns & Hocking, 1997). An increased risk of OSA is associated with male gender, increasing age, and being overweight. A middle aged, overweight male who snores loudly, has been witnessed by others choking, gasping, or having apneas (cessation of respiratory movement) during sleep and complains of excessive daytime sleepiness or insomnia likely has sleep apnea. It has been reported that commercial vehicle drivers have a higher incidence of OSA when compared to the general population (Horne & Reyner, 1995; Howard et al., 2001). Individuals who suffer from this disorder are statistically more likely to be involved in car crashes (George, Boudreau & Smiley, 1997; Young et al., 1997; Stoohs et al., 1994) and are potentially at a higher risk of other occupational accidents (Rodenstein, 2009). Notably, treatment of the OSA has been shown to reduce in motor vehicle accidents (Mazza, et al., 2006), highlighting the importance of early diagnosis and effective treatment of the disorder.

Age, gender, body mass index and neck circumference have been identified as independent predictors of sleep disordered breathing (Young et al., 2002). The Multivariable Apnea Prediction Scale (MAPS) (Maislin et al., 1995) is one screening tool that incorporates age, gender, body mass index and responses to three questions into a predictive equation for sleep disordered breathing. The questions relate to frequency of snorting or gasping; loud snoring; and episodes of choking, breathing stopping or struggling for breath at night. This questionnaire predicts sleep apnea risk using a score between zero and one (low to high probability of sleep disordered breathing), with relatively high sensitivity. In a clinical sample, the MAPS has been found to have a 95% sensitivity for detecting sleep disordered breathing (98% sensitivity for severe disease), with a specificity of 68%, as compared to PSG (Gurubhagavatula, et al., 2001).

Identification and treatment of OSA is an important part of reducing excessive sleepiness in workers, thereby reducing accident risk and increasing productivity in the workplace. Incorporated into an FRMS should be a mechanism for screening for those at-risk for OSA and other sleep disorders in order that the at-risk population can be formally evaluated with an overnight sleep study and, if diagnosed, treated. A two step screening process could involve an initial screening questionnaire such as the MAPS and, depending on available funding, those who were found to be at a higher risk for OSA could undergo nocturnal oximetry or overnight PSG recordings as further evaluation and/or formal diagnosis. Screening could be 1) routine as a part of a yearly physical exam, and/or 2) triggered by evidence of drowsiness or poor performance (by observation or added or embedded performance metrics) given adequate sleep opportunity and good use made of it. Similar recommendations have been made by the National Transportation Safety Board (NTSB) (http://www.ntsb.gov/recs/letters/2009/H09_15_16.pdf). Application of sleep apnea screening by Schneider Trucking according to Deborah Hersman, Chairman of the NTSB, “reduced preventable crashes by 30%, reduced the median cost of crashes by 48%, improved fleet retention rate by 60% over fleet average, and achieved health care savings of $539 per driver per month” (http://www.ntsb.gov/speeches/hersman/daph100526.html).

Evaluating effect of fatigue risk management implementations on error, incident, and accident, performance, and productivity

A fatigue risk management system is data driven. It operates on the principle of the process of iterative improvement dubbed “test, operate, test, exit (TOTE)” (Miller, et al., 1960), and the similar to the "observe, orient, decide, act (OODA) loop" posited by John Boyd (Coram, 2002; Wesensten, et al., 2005; http://en.wikipedia.org/wiki/John_Boyd_(military_strategist)). For fatigue risk management "test" involves monitoring of added or embedded measures of performance together with observation of error, incident, or accident; and/or loss of productivity and making absolute or relative comparisons to previous performance or some standard of performance, and thus detecting a drift away from nominal. "Operate" involves changing something in the system, e.g., the work schedule that operational experience suggests will correct the observed drift away from nominal performance. This is followed by another "test" to determine the effectiveness of "operate". This is an iterative process, repeating as many times as necessary until "test" yields nominal values, at which point the process exits. The iterative FRMS approach is qualitatively different from the promulgation of hours of service rules.

Error, incident, and accident reporting are fundamental to corporate safety management systems into which FRMS is logically folded. There is evidence that fatigue causes a decrease in productivity perhaps preceding an increase in error, incident, and accident, making loss of productivity a leading indicator (in the economic sense of early indicator) of fatigue (Thomas et al., 1997; Van Dongen, et al., 2010). Evaluating productivity and performance in the workplace is a critical component of fatigue risk management.

Summary of current practice and future promise of fatigue risk management

The current practice of fatigue risk management includes applying sleep science to reduce the risk of error, incident, or accident 1) within the context of the existing hours of service regulations and 2) by gaining exceptions to the existing regulations. For its future promise, fatigue risk management will replace the existing regulations (and labor management agreements) with sleep-science-derived mathematical models predicting individual and group performance from sleep/wake history, circadian rhythm phase, and workload derived from personal biomedical status monitoring integrated into rostering and scheduling software. Both the Federal Aviation Administration (FAA) and the International Civil Aviation Organization (ICAO) are putting forward proposals for the transition from hours of service (HOS) rules to fatigue risk management systems (FRMS). In the future, the model, informed by sleep and performance data, promises to become the rule.

References

Adams, N., Strauss, M., Schluchter, M., and Redline, S. (2001) Relation of measures of sleep-disordered breathing to neuropsychological functioning. *Am. J. Respir. Crit. Care Med.*, 163, pp. 1626-31.

Ancoli-Israel, S., Cole, R., Alessi, C., Chambers, M., Moorcroft, W., and Pollak, C.P. (2003) The role of actigraphy in the study of sleep and circadian rhythms. American Academy of Sleep Medicine Review Paper. *Sleep*, 26, no. 3, pp. 342-392.

Akerstedt, T. (2003) Shift work and disturbed sleep/wakefulness. *Occup. Med.*, 55, pp. 89-94.

Balkin, T.J., Bliese, P.D., Belenky, G., Sing, H., Thorne, D.R., Thomas, M., Redmond, D.P., Russo, M., and Wesensten, N.J. (2004) Comparative utility of instruments for monitoring sleepiness-related performance decrements in the operational environment. *J. Sleep Res.* 13, pp. 219-227.

Basner, M., Fomberstein, K.M., Razavi, F. M., Banks, S., William, J.H., Rosa, R.R., and Dinges, D.F. (2007) American time use survey: Sleep time and its relationship to Waking Activities. *Sleep*, 30, no. 9, pp. 1085-1095.

Belenky, G. and Akerstedt, T. (in press) Introduction to occupational sleep medicine. In M. Kryger, T. Roth, and W.C. Dement (Eds.) *Principles and Practice of Sleep Medicine*, 5th Edition.

Belenky, G., Hursh, S.R., Fitzpatrick, J. (2008) Split sleeper berth use and driver performance: a review of the literature and application of a mathematical model predicting performance from sleep/wake history and circadian phase. Report prepared for The American Trucking Associations, Sleep and Performance Research Center, Washington State University, Spokane, WA.

Belenky, G., Marcy, S.C., and Martin, J.A. (1996) Debriefings and battle reconstructions following combat. In J.A. Martin, L. Sparacino, and G. Belenky (Eds.) *The Gulf War and Mental Health: A Comprehensive Guide*, Praeger, Westport, CT.

Belenky G., Wesensten N.J., Thorne, D.R., Thomas, M.L., Sing, M.L., Redmond, D.P., Russo, M.B., and Balkin, T.J. (2003) Patterns of performance degradation and restoration during sleep restriction and subsequent recovery: a sleep dose-dependent study. *J. Sleep Res.*, 12, pp. 1-12.

Bierman, A., Klein, T.R., and Rea, M.S. (2005) The daysimeter: A device for measuring optical radiation as a stimulus for the human circadian system. *Meas. Sci. Technol.*, 16, pp. 2292-2299.

Bliese, P.D., Wesensten, N.J., and Balkin, T.J. (2006) Age and individual variability in performance during sleep restriction. *J. Sleep Res.*, 15, no. 4, pp. 376-385

Bonnet, M.H. and Arand, D.L. (2003) Clinical effects of sleep fragmentation versus sleep deprivation. *Sleep Med. Rev.*, 7, no. 4, pp. 297-310.

Carskadon, M.A., Dement, W.C., Mitler, M.M., Roth, T., Westbrook, P.R., and Keenan, S. (1986) Guidelines for the multiple sleep latency test (MSLT): A standard measure of sleepiness. *Sleep*, 9, no. 4, pp. 519-524.

Carskadon, M.A. and Dement, W.C. (1981) Respiration during sleep in the aged human. *J. Gerontol.*, 36, pp. 420-23.

Coram, R. (2002) *Boyd: The Fighter Pilot Who Changed the Art of War*. Little, Brown, New York.

Cornish, W.R. and Clark, G. (1989) *Law and Society in England 1750-1950*. Sweet Maxwell, London.

Costa, G., Akerstedt, T., Nachreiner, F., Baltieri, F., Folkard, S., Dresen, M.F., Gadbois, C., Gartner, J., Sukalo, H.G., Marma, M., Kandolin, I., Silverio, J., and Simoes, A. (2004) Flexible working hours, health, and well-being in Europe: some considerations from a SALTSA project. *Chronobiol. Int.*, 21, pp. 831-844.

Dawson, D. and McCulloch, K. (2005) Managing fatigue: it's about sleep. *Sleep Med. Rev.*, 9, pp. 365-380.

Dembe, A. Erickson, J., Delbos, R., and Banks, S. (2005) The impact of overtime and long work hours on occupational injuries and illnesses: new evidence from the United States. Occup. Environ. Med. 2005 September; 62(9): 588–597

Dorrian, J., Rogers, N.L. and Dinges, D.F. (2005). Psychomotor vigilance performance: neurocognitive assay sensitive to sleep loss. In Kushida, C.A. (Ed.). *Sleep Deprivation: Clinical issues, pharmacology, and sleep loss effects.* New York: Marcel Dekker, pp. 39–70.

Edwards, B., Waterhouse, J., Reilly, T., and Atkinson, G. (2002) A comparions fo the suitabilities of rectal, gut, and insulated axilla temperatures for measurement of the circadian rhythm of core temperature in field studies. *Chronobiol. Int.*, 19, no. 3, pp. 579-598.

Folkard, S., and Tucker, P. (2003) Shift work, safety, and productivity. *Occup. Med.,* 53, pp. 89-94.

Gander, P.H, Graeber, R.C., and Belenky, G. (in press) Fatigue Risk Management. In Kryger, M., Roth, T. and Dement, W.C. (Eds.) *Principles and Practice of Sleep Medicine,* 5th Edition, Elsevier, Philadelphia, PA.

George, C.F., Boudreau, A.C., and Smiley, A. (1997) Effects of nasal CPAP on simulated driving performance in patients with obstructive sleep apnoea. *Thorax*, 52, no. 7, pp. 648-653.

Gurubhagavatula, I., Maislin, G., and Pack, A.I. (2001) An algorithm to stratify sleep apnea risk in a sleep disorders clinic population. *Am. J. Respir. Crit. Care Med.*, 164, pp. 1904-1909.

Harrison, Y. and Horne, J.A. (2000) The impact of sleep deprivation on decision making: a review. *J. Exp. Psychol. Appl.*,6, no. 3, pp. 236-249.

Hersman, D. (2010) Remarks of Honorable Deborah A.P. Hersman, Chairman, National Transportation Safety Board Before The National Sleep Foundation, Washington, DC March 5, 2010, http://www.ntsb.gov/speeches/hersman/daph100305.html.

Horne, J.A. and Reyner, L.A. (1995). Sleep related vehicle accidents. *Br. Med. J.*, 310, no. 6979, pp. 565-567.

Howard, M., Worsnop, C., Campbell, D., Swann, P., and Pierce, R. (2001) Sleep disordered breathing in Victorian transport drivers. *Am. J. Respir. Crit. Care Med.*, 163, no. 5, pp. A933.

Jewett, M.E., Dijk, D.J., Kronauer, R.E., and Dinges, D.F. (1999) Dose-response relationship between sleep duration and human psychomotor vigilance and subjective alertness. *Sleep*, 22, no. 2, pp. 171-179.

Johns, M.W. (1993) Daytime sleepiness, snoring, and obstructive sleep apnea. The Epworth Sleepiness Scale. *Chest,* 103, no. 1, pp. 30-36.

Johns, M. and Hocking, B. (1997) Daytime sleepiness and sleep habits of Australian workers. *Sleep*, 20, no. 10, pp.844-849.

Knutson, K.L., Spiegel, K., Penev, P., and Van Cauter, E. (2007) The metabolic consequences of sleep deprivation. *Sleep Med. Rev.*, 11, pp. 163-178.

Lauderdale, D.S., Knutson, K.L., Yan, L.L., Rathouz, P.J., Hulley, S.B., Sidney, S., and Kiang, L. (2006) Objectively measured sleep characteristics aomon early-middle-aged adults: The cardia study. *Am. J. Epidemiology*, 164, no. 1, pp. 5-16.

Lavie, P. (1983) Incidence of sleep apnea in a presumably healthy working population: a significant relationship with excessive daytime sleepiness. *Sleep*, 6, pp. 312-318.

Lewy, A.J. and Sack, R.L. (1989) The dim light melatonin onset as a marker for circadian phase position. *Chronobiol. Int.*, 6, no.1, pp 93-102.

Lockley S.W., Brainard, G.C., and Czeisler, C.A. (2003) High sensitivity of the human circadian melatonin rhythm to resetting by short wavelength light. *J. Clin. Endocrinol. Metab*., 88, no. 9, pp. 4502-4505.

McDonald, J.L., Lillis, T.A., Tompkins, L.A., Van Dongen, H., and Belenky, G. (2008) Effects of extended work hours on objectively measured sleep and performance in industrial employees. *Sleep*, 31, pp. A374.

McDonald, J.L., Tompkins, L.A., Lillis, T.A., Bowen, A.K., Grant D.A., Van Dongen, H.P.A., and Belenky, G. (2009) Work hours, sleep, and performance in medical residents working night float vs. day shift. *Sleep*, 32, pp. A394.

McDonald, J., Patel, D., and Belenky, G. (in press) Sleep and performance monitoring in the workplace: The basis for fatigue risk management. In M. Kryger, T. Roth, and W.C. Dement (Eds.) *Principles and Practice of Sleep Medicine*, 5th Edition, Elsevier, Amsterdam.

Magistretti, P.J., Pellerin, L., and Martin, J.L. (1995) Brain energy metabolism, an integrated cellular perspective. In F.E. Bloom and D.J. Kupfer (Eds.) *Psychopharmcology: The Fourth Generation of Progress.* Raven Press Ltd., New York, pp. 657-670.

Maislin, G., Pack, A.I., Kribbs, N.B., Smith, P.L., Kline, L.R., Schwab, R.J., and Dinges, D.F. (1995) A survey screen for prediction of apnea. *Sleep*, 18, no. 3, pp. 158-166.

Mallis, M.M., Mejdal, S., Ngyuen, T.T., and Dinges, D.F. (2004) Summary of the key features of seven biomathematical models of human fatigue and performance. *Aviat. Space Environ. Med.*, 75, pp. A4-A14.

Mazza, S., Pepin, J.L., Naegele, B., Rauch, E., Deschaux, C., Ficheux, P., and Lévy, P. (2006) Driving ability in sleep apnoea patients before and after CPAP treatment: evaluation on a road safety platform. *Eur. Respir. J.*, 28, pp. 1020-1028.

Meier-Ewert, H.K., Ridker, P.M., Rifai N., Price, N., Dinges, D., and Mullington, J. (2004) Effect of sleep loss on c-reactive protein, an inflammatory marker of cardiovascular risk. *J. Am. Coll. Cardiol.*, 43, pp. 678-683.

Miller, G., Galanter, E., and Pribram, K. (1960) *Plans and the structure of behavior*. Holt, Rinehart and Winston, New York.

Moore, R.Y. (1997) Circadian rhythms: Basic neurobiology and clinical applications. *Annu. Rev. Med.*, 48, pp. 252-266.

Moore, R.Y., Speh, J.C., and Leak, R.K. (2002) Suprachiasmatic nucleus organization. *Cell Tissue Res.*, 309, pp.89-98.

Moore-Ede, M. (1995) Things that go bump in the night. *American Bar Association J.* 81, January, pp 56-60.

Mullington, J.M., Haack, M., Toth, M., Serrador, J.M., and Meier-Ewert, H.K. Cardiovascular, inflammatory, and metabolic consequences of sleep deprivation. *Prog. Cardiovasc. Dis.* , 51, no. 4, pp. 294-302.

Nilsson, J.P., Soderstrom, M., Karlsson, A.U., Lenader, M., Akerstedt, T., Lindroth, N.E., and Axelsson, J. (2005) Less effective executive functioning after one night's sleep deprivation. *J. Sleep Res.*, 14, no. 1, pp. 1-6.

Olofsen E., Dinges D.F., and Van Dongen H.P.A. (2004) Nonlinear mixed effects modeling: individualization and prediction. *Aviat. Space Environ. Med.*, 75, no. 3, Suppl., pp. A134–A140.

Perrow, C. (1999) *Normal accidents.* Princeton: Princeton University Press.

Petrilli, R.M., Thomas, M.J.W., Lamond, N., Dawson, D., and Roach, G. (2007) Effect of flight duty and sleep on the decision-making of commercial airline pilots. In J.M. Anca (Ed.) *Multimodal Safety Management and Human Factors: Crossing the Borders of Medical, Aviation, Road and Rail Industries.* Ashgate Publishing Company Ltd., Burlington, Vermont, pp. 259-270.

Petrie, K.J., Powell, D.M.C., and Broadbent, E.A. (2004) Fatigue self-management strategies and reported fatigue in international pilots. *Ergonom.*, 47, no. 5, pp. 461-468.

Philip, P., Sagaspe, P., Taillard, J., Valtat, C., Moore, N., Akerstedt, T., Charles, A., and Bioulac, B. (2005) Fatigue, sleepiness, and performance in simulated versus real driving conditions. *Sleep*, 28, no. 12, pp. 1511-1516.

Powell, D., Spencer, M., Holland, D., and Petrie, K. (2008) Fatigue in two-pilot operations: implications for flight and duty time limitations. *Aviat. Space Environ. Med*., 79, no. 11, pp. 1047-1050.

Rodenstein, D. (2009) Sleep apnea: traffic and occupational accidents--individual risks, socioeconomic and legal implications. *Respiration*, 78, no. 3, pp. 241-248.

Romig, E., and Klemets, T. (2009) Fatigue risk management in flight crew scheduling. *Aviat. Space Environ. Med*., 80, no. 12, pp. 1073-1074.

Rupp, T.L., Wesensten, N.J., Bliese, P.D., and Balkin, T.J. (2008) Banking sleep: Realization of benefits during subsequent sleep restriction. *Sleep*, 32, no. 3, pp. 311-321.

Samn, S.W. and Perelli, L.P. (1982) Estimating aircrew fatigue: A technique with implications for airlift operations. *Tech Rep SAM-TR-82-21*, USAF School of Aerospace Medicine, Brooks AFB, TX.

Stoohs, R.A., Guilleminault, C., Itoi, A., and Dement, W.C. (1994) Traffic accidents in commercial long-haul truck drivers: the influence of sleep-disordered breathing and obesity. *Sleep*, 17, no. 7, pp. 619-623.

Thomas, G.R., Raslear, T.G., and Kuehn, G.I. (1997) The effects of work schedule on train handling performance and sleep of locomotive engineers: A simulator study. *Final Report, DOT/FRA/ORD-97-09*, Federal Railroad Administration, U.S. Department of Transportation, Washington, D.C.

Thomas, M.L., Sing, H.C., Belenky, G., Holcomb, H., Mayberg, H., Dannals, R., Wagner, H., Thorne, D., Popp, K., Rowland, R., Welsh A., Balwinski, S., and Redmond, D.P. (2000) Neural basis of alertness and cognitive performance impairments during sleepiness. I. Effects of 24 h of sleep deprivation on waking human regional brain activity. *J. Sleep Res.*, 9, no. 4, pp. 335-352.

Thorne, D.R., Genser, S., Sing, H., and Hegge, F. (1983) Plumbing human performance limits during 72 hours of high task load. *In Proceedings of the 24th DRG Seminar on the Human as a Limiting Element in Military Systems*. Defense and Civil Institute of Environmental Medicine (DCIEM), Toronto, Canada, pp.17-40.

Tucker, A.M., Whitney, P,, Belenky, G., Hinson, J.M., and Van Dongen, H.P.A. (2010) Effects of sleep deprivation on dissociated components of executive functioning. *Sleep*, 33, no. 1, pp. 47–57.

Van Cauter, E., Spiegel, K., Tasali, E. and Leproult, R. (2008) Metabolic consequences of sleep and sleep loss. *Sleep Med.*, 9 Suppl., pp. S23-S28.

Van Dongen, H., Belenky, G., Moore, J.M., Bender, A.M., Huang, L., Mott, C.G., and Vila, B.J. (2010) Nighttime driving and fuel use: a high-fidelity simulator study in a sleep laboratory. *Sleep*, 33, pp. A308.

Van Dongen, H.P.A., Belenky, G., and Krueger, J.M. (2010) Investigating the temporal dynamics and underlying mechanisms of cognitive fatigue. In P.L. Ackerman (Ed.) *Cognitive Fatigue: Multidisciplinary Perspectives on Current Research and Future Applications.* American Psychological Association, Washington, D.C.

Van Dongen, H.P.A., Maislin, G., Mullington, J.M., and Dinges, D.F. (2003) The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. *Sleep*, 26, no. 2, pp. 117-126.

Van Dongen, H.P.A., Vitellaro, K.M. and Dinges, D.F. (2005) Individual differences in adult human sleep and wakefulness: Leitmotif for a Research Agenda. *Sleep*, 28, no. 4, 1-18.

Viola, A.U., Archer, S.N., James, L.M., Groeger, J.A., Lo, J.C.Y., Skene, D.J., von Shantz, M.J., and Dijk, D-J. (2007) PER3 Polymorphism predicts sleep structure and waking performance. *Curr. Biol.*, 17, pp. 613-618.

Webb, W.B. and Dinges, D.F. (1989) Cultural perspectives on napping and the siesta. In D.F. Dinges and R.J. Broughton (Eds.) *Sleep and Alertness: Chronobiological, Behavioral, and Medical Aspects of Napping*. Raven Press, New York, pp. 247-265.

Wesensten, N.J., Belenky, G., Thorne, D.R., Kautz, M.A., and Balkin, T.J. (2004) Modafinil versus caffeine: Effects on fatigue during sleep deprivation. *Aviat. Space Environ. Med.*, 75, pp. 520-525.

Wesensten, N.J., Belenky, G. and Balkin, T.J. (2005) Cognitive readiness in network centric operations. *Parameters: U.S. Army War College Quarterly*, 35, no. 1, pp. 94-105.

Wright, K.P., Gronfier, C., Duffy, J.F., Czeisler, C.A (2005). Intrinsic period and light intensity determine the phase relationship between melatonin and sleep in humans. *J. Biol. Rhythms*, 20, no.2, pp. 168–177.

Young, T., Blustein, J., Finn, L., and Palta, M. (1997). Sleep-disordered breathing and motor vehicle accidents in a population- based sample of employed adults. *Sleep*, 20, no. 8, pp. 608-613.

Young, T., Shahar, E., Nieto, F.J., Redline, S., Newman, A.B., Gottlieb, D.J., Walsleben, J.A., Finn, L., Enright, P., and Samet, J.M. (2002) Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. *Arch. Intern. Med.*, 162, pp. 893-900.